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Bacteriologic follow-up of schoolgirls with untreated covert bacteriuria. *A. W. Asscher, E. R. Verrier-Jones, Kate Verrier Jones, Ruth Mackenzie, and L. A. Williams. K.R.U.F. Institute of Renal Disease, Welsh National School of Medicine, Royal Infirmary, Cardiff, Wales.* Midstream urine specimens were obtained at approximately 2-month intervals over a 4-year period from 75 schoolgirls aged 5 to 12 years, with untreated covert bacteriuria. At the start, *Escherichia coli* strains were isolated from all patients from catheter specimens of urine obtained during voiding cystourography. In 16 (21%) of the 75 girls, a spontaneous cure of bacteriuria occurred mostly within the first year of the detection of bacteriuria and mostly in girls in whom the urinary tract was radiologically normal. In 22 (29%) of the girls, bacteriuria persisted throughout follow-up. The organisms were identical in serotype in 7, and changed serotype or even species in 15. In 13 of the 22 girls with persistent bacteriuria, kidney scarring, or vesico-ureteric reflux (VUR), or both, were present initially. Progression of this kidney damage tended to occur more so in the girls in whom VUR and persistent infection due to changing pathogens were found. Thirty seven (50%) of the girls had intermittent bacteriuria during follow-up. In 19 of these in whom more than 15 isolates were available, a study of the sensitivity of the organisms to the cidal effect of serum was undertaken by Professor L. A. Hanson and Dr. S. Olling of the Department of Immunology, University of Göteborg. In these 19 girls, 36 episodes of spontaneous clearance of bacteriuria followed by reinfections took place. In 26 of these episodes, the *E. coli* strain was highly sensitive to the cidal effect of human serum before the urine became sterile. This suggests that spontaneous clearance of urinary tract infection depends on changes in the surface structure of *E. coli* induced by natural defensive mechanisms.

Complex dissolution: An assay for complement function and immune-complex load. *S. R. Bartolotti, B. Pussell, A. Dash, and D. K. Peters. Renal Unit, Royal Postgraduate Medical School, Hammersmith Hospital, London, England.* Recent observations on a new function of complement (C) have led us to assess it in patients with diseases associated with circulating immune complexes (CIC). It has been reported that antigen-antibody precipitates can be dissolved in vitro into small complexes under the influence of C and that cobra venom factor-induced hypocomplementaemia in rabbits with acute serum sickness results in delayed clearance of complexes from the glomerulus. This function of C was examined in 170 patients using a simple radioimmunoassay: precipitates made of radioiodinated bovine serum albumin and rabbit antibody were incubated in the presence of test serum for 1 hour at 37° C. The fraction of complexes solubilized by complement from the precipitate was expressed as a percentage of the total radioactivity added. Abnormally low values were found in patients with hypocomplementaemia, CIC (Clq binding assay), and also in some patients in whom the complement profile was normal and CIC undetectable. Sequential studies have been performed in patients with SLE (9), vasculitis (3), and glomerulonephritis (5). A persistent abnormality of complex dissolution was associated with continuing disease and returned to normal with clinical remission. This is a simple assay that measures functional complement in one step and when combined with calcium chelation also assays the alternative pathway. It is able to discriminate between complement-solubilized and complement-activating immune complexes as well as to detect anti-complementary reactants. As it appears to be associated with disease activity, it may be useful in patient management.

Release of vascular permeability factor from lymphocytes of patients with minimal change nephropathy. *M. Boulton-Jones and S. Simpson. Kidney Diseases Research Unit, Royal Infirmary, Glasgow, Scotland.* The pathogenesis of minimal change nephropathy (MCN) is unknown, but some clinical and experimental observations suggest that the role of lymphocytes may be important. The effect of tuberculosis, which is a potent stimulator of cell-mediated immunity, on the natural history of a patient with MCN would be of interest and will be described. It has been postulated that the lymphocytes of patients with MCN release a factor (lymphokine) which increases vascular permeability, thus causing proteinuria. We attempted to test this hypothesis by culturing peripheral blood lymphocytes. Phytohaemagglutinin (PHA) was added to the stimulated (S) cultures, and saline to control (R) cultures. The supernatant was harvested after 24 to 48 hours and assayed for vascular permeability by the Evans Blue technique. The results were: Mean area of reconstituted supernatant of control subjects (R_1) was 32.8 mm² ($N = 10$); mean area of reconstituted supernatant of MCN patients (R_2) was 105.4 mm² ($N = 7$); mean area of stimulated supernatant of control subjects (S_1) was 60.2 mm² ($N = 10$); mean area of stimulated supernatant of MCN patients (S_2) was 113.8 mm² ($N = 7$). The cells for these experiments were taken during relapse. Similar experiments failed to show any difference between the cells of patients taken during remission and the control group. These results suggest that lymphocytes of patients with MCN produce abnormal amounts of vascular permeability factor during relapse even in the absence of an in vitro stimulant, presumably because they have already been stimulated in vivo.

Serum ferritin concentration and oral iron therapy in patients on regular hemodialysis. *A. M. Cotterill, J. N. Flather, W. R. Cattell, M. D. Barnett, and L. R. I. Baker. Department of Nephrology, St. Bartholomew's Hospital, London, England.* Serum ferritin concentration was measured in 61 hemodialysis patients receiving "low" (60 to 120 mg, $N = 15$), "intermediate" (121 to 240 mg, $N = 28$) or "high" (241 to 360 mg, $N = 18$) oral intakes of elemental iron daily. Only 3 patients had ever received parenteral iron, and none had received parenteral iron within the previous 12 months. Mean serum ferritin concentration was 493 μg/liter (range, 10 to 8600; normal range, 15 to 250 μg/liter). Serum ferritin was elevated in 44 patients, normal in 16, and reduced in one. This last patient used a coil dialyzer whereas the remaining 60 used flat board dialyzers. Mean serum ferritin concentration was significantly lower in the group receiving the "low" intake

of iron than it was in each of the other two groups ($P < 0.001$ in each instance). We conclude that it is unnecessary to exceed 120 mg of elemental iron daily to maintain iron balance in patients treated by flat board hemodialysis provided that economy in blood sampling is exercised. This dose is too large in some patients. We suggest an adequate maintenance dose for the majority of patients to be 60 mg of elemental iron (one ferrous sulphate tablet) daily.

Goodpasture's syndrome: Radioimmunoassay for measurement of circulating anti-GBM antibody. *C. M. Lockwood, N. Amos, and D. K. Peters. Renal Unit, Royal Postgraduate Medical School, Hammersmith Hospital, London, England.* Using a collagenase extract of glomerular basement membrane (GBM), we have developed a robust and sensitive solid-phase radioimmunoassay to detect circulating antibodies to GBM in patients with clinical and histologic features of anti-GBM nephritis. The technique relies on the binding of the collagenase extract to the wall of a plastic tube and subsequent fixation of specific antibody from diluted samples of patients' serum. By using a highly purified ^{125}I-labeled goat antihuman IgG, we found the degree of binding to be related to that produced by a standardized antibody eluted from the kidney of a patient with anti-GBM nephritis. The binding is less than 10% for patients with other forms of nephritis but may be as high as 80% for patients with severe anti-GBM disease. Using this technique we have so far documented 40 patients with anti-GBM nephritis confirmed by renal biopsy. The application of this assay in the management of patients presenting with severe nephritis and the subsequent monitoring of therapy are discussed.

Urinary excretion of the Tamm-Horsfall glycoprotein in normal subjects and in patients after renal transplant. *R. D. Marshall and A. Goodall. Department of Biochemistry, University of Strathclyde, Glasgow, and Department of Chemical Pathology, St. Mary's Hospital Medical School, London, England.* The Tamm-Horsfall urinary glycoprotein is of considerable interest even though we do not fully understand its functions. It is produced by the luminal cells of the ascending limb of Henle's loop and of the distal convoluted tubule. Production of the apoprotein on the polysomes of the renal cells is followed by a complex series of glycosylation reactions as the molecule travels through the cisternae of the endoplasmic reticulum and Golgi's complex to reach what appears to be the site of the predominant location, associated with the plasma membrane. It is present on both the tubular luminal surface and on the basal plasma membrane, including its invaginations. The glycoprotein may be directly involved in the development and maintenance of the hyperosmolarity of the renal medulla. There is release of Tamm-Horsfall glycoprotein from the tubular cells into the tubular urine which appears, at least in part, in voided urine. We have made measurements of the glycoprotein in urine by a radioimmunoassay procedure, and these assays are best done on urine samples which have been dialyzed against water and freeze-dried. This is because freeze-dried Tamm-Horsfall glycoprotein reacts more effectively with antibody than does glycoprotein which has not been subjected to freezing or freeze-drying, and this is true for antibody raised against either freeze-dried antigen or nonfrozen antigen. Thus, solutions of Tamm-Horsfall glycoprotein, when radioimmunoassayed using a freeze-dried standard, appear to contain only 6% of the true content. Slow freezing (10 to 30 min at 20° C) increases this to 40%, quick freezing CO_2/methanol, shell freezing (30 to 60 s) to 62%, and freeze drying to the correct value. The daily excretion of the glycoprotein by a normal subject does not change even if the volume of urine varies by up to a factor of 2, and the total amount is apparently unrelated to the volume of urine. The results obtained with renal transplant patients indicated that the excretion of Tamm-Horsfall glycoprotein does not necessarily begin with excretion of urine. The data appear to fall into two groups. In the first, the urinary output of the glycoprotein was found to increase as creatinine clearance rose. None of these patients suffered a rejection episode over the period of time that we were able to follow the urinary excretion of the Tamm-Horsfall glycoprotein. In the other groups, all had indications of rejection of the allograft within a relatively short period of time after transplantation. The amount of Tamm-Horsfall glycoprotein excreted increased before the rejection episode and fell during it.

Studies on mesangiocapillary glomerulonephritis in Finnish Landrace sheep. *C. P. Swainson and D. Thomson. The Medical Renal Unit, Department of Medicine and the Pathology Department, University of Edinburgh, Scotland.* A spontaneous mesangiocapillary glomerulonephritis (MCGN) in young Finnish Landrace lambs was described in 1974, and it was noted that this disease was almost identical to human MCGN. The human disease is often associated with persistent hypocomplementaemia and the presence of the C3 nephritic factor. Persistent low serum C3 levels from birth are seen in those lambs who will die from renal failure 6 to 8 weeks later. Sibling lambs with normal C3 levels do not develop the disease, and the frequency of the disease depends on a particular ram mating with "high-risk" ewes. During the past two breeding seasons we have attempted to modify the course of the disease using immunosuppressive drugs. From a total of 62 live births, we identified 16 affected lambs with severe hypocomplementemia. Blood was drawn within 12 hours of birth, and C3 results were known the following day. Prednisone (40 mg) and cyclophosphamide (5 mg/kg), orally, was started and continued for 8 weeks or until death. We attempted to transmit the disease from affected lambs to healthy siblings by twice-weekly injections of 1 ml of serum. C3 was estimated weekly. Postmortem examinations with renal histology were performed on every lamb which died and renal biopsies on the survivors at 12 weeks. Mean plasma C3 level for affected lambs was 4.3 ± 1.5% of that of controls and 61 ± 22% and 52 ± 27% for unaffected siblings and normal lambs, respectively. Three lambs survived the experiments, and the mean survival of the others was 62 days, a little longer than that for previously untreated lambs, but 5 of these died from infection and did not have advanced renal disease at death. The surviving lambs showed only minor glomerular disease. Serum C3 in treated affected animals rose to 12.1 ± 13% of controls and rose into the normal range in all those who survived for more than 6 weeks. No lambs given serum from diseased lambs showed any change in complement levels, but two had advanced MCGN when sacrificed. These results indicate possible modification of the disease and of the hypocomplementemia by immunosuppression, but the drugs used also contributed to the high mortality.

Does the nephrotic syndrome increase the risk of cardiovascular disease? *V. J. Wass, R. J. Jarrett, and J. S. Cameron. Renal Unit and Department of Community Medicine, Guy's Hospital, London, England.* A markedly increased incidence of ischemic heart disease (IHD) has been reported in patients with nephrotic syndrome (NS), but this conclusion was based on two very small, highly selected series. We therefore followed up all adults who presented with NS in the S.E. Thames Region between January 1972 and December 1975. Diabetics and patients aged < 15 years at presentation were excluded. Every patient was traced. If deceased, the cause of death was established from postmortem data and hospital notes. If alive, they were asked to : (*a*) complete a standard questionnaire to assess symptoms of angina and intermittent claudication, (*b*) have a 12-lead resting electrocardiogram (ECG) and, (*c*) attend fasting for measurement of plasma lipids and glucose tolerance. One hundred fifty-nine adult nephrotics (mean age ± [SD] 49.0 ± 17.1 years) were followed for a mean of 4.9 years (total group follow-up, 784 years). Forty nine (31%) were dead or had nonfunctioning kidneys (mean age, 53.0 ± 17.4 years); of these, 8 were alive on dialysis or transplant programs; 21 had died in chronic renal failure, and 20 from other causes, which included 4 deaths from IHD. This incidence of death from IHD does not differ significantly from that in the general population. One hundred eight patients (68%) were alive (mean age, 47.4 ± 16.7 years). Fifty nine had had continuous and 37 intermittent proteinuria, and 12 one episode of proteinuria only (< 6 months) over the follow-up period. Two cases remain

untraced. To date, 104 questionnaires and 73 ECGs have been completed. For each sex and age decade, the incidence of angina, intermittent claudication, or ischemic ECG abnormality are not significantly different from a control population. Known risk factors for IHD were also assessed at follow-up. Hypertension was present in 33% of the nephrotic patients. Total plasma cholesterol was elevated in 34% and total plasma triglyceride in 19%. High-density lipoprotein (HDL) cholesterol levels were, however, normal in all patients studied to date. Glucose tolerance was not impaired. Thus after a mean follow-up of 4.9 years, an increased incidence of cardiovascular disease could not be detected in this predominantly middle-aged population of patients presenting with nephrotic syndrome. Hypertension was significantly increased, but HDL cholesterol levels were normal. Routine treatment of hyperlipidemia in unselected adult nephrotics is not indicated.

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New method of water treatment for hemodialysis. *A. Abadie, P. Bec, J. M. Pujo, J. L. Lacombe, F. Malha, D. Marty, and M. Mustin. Clinique Saint-Exupéry, Toulouse, France.* Since July 1977, French pharmacopoeia has recommended that water used in hemodialysis contain limited quantities of anions and cations. With the exception of total demineralization and distillation, no current procedure meets these specifications. Particularly conspicuous in this regard is the softening technique, which is acceptable with regard to cations but not with regard to anions. However, this shortcoming can be eliminated by combining the softening procedure with an anionic permutation reaction. All anions, particularly those most prohibited, NO_3^-, NO_2^-, F^-, are eliminated from the water and replaced by equivalent quantities of CH_3COO^- ions. This reaction also occurs using an ion exchanger according to the equation:

$$R^+CH_3COO^- + F^- \rightarrow \underset{\text{Resin}}{R^+F^-} + CH_3COO^-$$

Inflowing anionic salts are totally transformed into CH_3COO^- ions. In addition, this anion is used for the dialysate at approximately 35 mEq/liter and its desorption in front of all water anions is very easy. Regarding the technical aspects: *(1)* the process is combined in the same column with softening resin, *(2)* the regeneration of the two functions is achieved simultaneously by means of a sodium acetate brine. The obtained results, using a prototype, are presented along with a perspective concerning application in hemodialysis and peritoneal dialysis.

HDL cholesterol as cardiovascular risk factor in uremia. *F. Delavelle, J. C. Trombert, and G. Canarelli. Service de Néphrologie, Centre Rénal Ermitage, Evian les Bains, France.* HDL cholesterol levels were studied concurrently with "standard" blood lipid analysis in 105 subjects subdivided into three groups: *(1)* healthy subjects (34 cases), *(2)* patients with severe renal failure (serum creatinine, 60 to 100 mg/liter) (18 cases), *(3)* chronic hemodialyzed patients (53 cases). Hypertriglyceridemia was a predominant feature in group 2 (22% of cases with a mean range of 2.60 ± 0.59 g/liter) and group 3 (21% of patients; mean range, 2.40 ± 0.75 g/liter). Its incidence was reduced in African hemodialyzed patients but was not influenced by sex, age, or carbohydrate and caloric intake (although triglyceridemia was in the normal range positively correlated with carbohydrate intake: $r = +0.56$, $P < 0.01$). Total blood cholesterol was normal in the three groups, but HDL cholesterol and the α/β cholesterol ratio was significantly reduced ($P < 0.001$) in groups 2 (respectively, 0.32 ± 0.11 and 0.21 ± 0.08 g/liter) and 3 (0.39 ± 0.11 and 0.27 ± 0.12 g/liter) as compared to group 1 (0.54 ± 0.15 and 0.42 ± 0.21 g/liter). This drop in cholesterol was more pronounced in males but was not related to age, ethnic origin, or the presence of dyslipidemia according to Frederickson's classification (HDL cholesterol, 0.42 ± 0.14 g/liter in type IV dyslipidemia and 0.40 g/liter in hemodialyzed patients without dyslipidemia). However, we found a positive correlation ($r = 0.80$, $P < 0.05$) between nerve conduction velocity and HDL cholesterol, and cholesterol was significantly decreased ($P < 0.01$) in group 2 (0.32 ± 0.11 g/liter) when compared to the dialyzed patients in group 3 (0.39 ± 0.11 g/liter). We suggest that better adequacy of dialysis may decrease cardiovascular risk in uremic patients by increasing HDL cholesterol serum level.

Continuous peritoneal dialysis in the treatment of end-stage renal failure. *M. Dratwa, P. Vereerstraeten, and C. Toussaint. Département de Néphrologie, Cliniques Universitaires de Bruxelles, Hôpital Brugmann and Hôpital Erasme, Bruxelles, Belgium.* Three patients with end-stage renal failure with residual creatinine clearance under 2 ml/min were treated by continuous peritoneal dialysis (CPD), as advocated by Popovich, with four 2-liter exchanges per day, 5 days per week. As each patient had been previously treated by hemodialysis (HD) and/or intermittent peritoneal dialysis (IPD), it was possible to compare the efficiency of CPD to that of conventional methods. The table shows the serum concentrations (mean + SEM) of urea, creatinine, uric acid, phosphorous, and proteins observed in the three patients in the course of the different modes of therapy used.

Patient	Urea *mg/dl*	Creatinine *mg/dl*	Uric acid *mg/dl*	Phosphorus *mg/dl*	Proteins *g/dl*
Patient 1 (female, 73 yr)					
IPD 208 days	201 ± 6.5	7.7 ± 2.2	11.9 ± 2.6	5.2 ± 2.8	6.7 ± 0.9
CPD 22 days	109 ± 9.0	6.8 ± 3.1	8.3 ± 3.2	3.0 ± 1.4	5.4 ± 1.1
Patient 2 (female, 57 yr)					
IPD 116 days	179 ± 9.0	11.0 ± 0.4	10.7 ± 0.6	4.1 ± 0.3	6.1 ± 0.3
CPD 28 days	56 ± 5.0	6.1 ± 0.3	5.5 ± 0.3	2.0 ± 0.2	4.9 ± 0.1
Patient 3 (male, 59 yr)					
HD 335 days	157 ± 9.7	14.3 ± 8.1	11.2 ± 6.6	5.7 ± 4.9	6.5 ± 0.9
IPD 82 days	181 ± 15.8	16.0 ± 7.4	14.0 ± 4.4	5.6 ± 3.2	5.7 ± 2.0
CPD 28 days	63 ± 7.6	8.1 ± 3.6	6.7 ± 2.3	3.2 ± 1.7	4.4 ± 1.8